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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of: ZYBIN D.V., KOTELEVITS A.G., SEVERIN S.E., SOLOGUB V.K.

Serial No. US No. 09/890,496

Filing date: July 31, 2001

For: USE OF POLYACRYLAMIDE GEL FOR FORMING A CAPSULE IN THE TISSUE OF THE ORGANISM OF A MAMMAL, AND A METHOD OF CULTIVATING CELLS, AND A METHOD OF TREATING ONCOLOGICAL DISEASES AND DIABETES MELLITUS

DECLARATION UNDER 37 C.F.R. § 1.132

I, the undersigned, Oleg Vladimirovich Matorin, hereby declare that:

1. I am a citizen of Russia, resident of Moscow, 117279, ul. Mikloukho-Maklaya, 51, corp. 2, apt. 73;

2. I graduated from 2nd Moscow Order of Lenin State Medical Institute named after Pirogov (presently – Russian State Medical University) in 1992.

3. I am currently employed at Moscow P.A. Gerzen Research Institute of Oncology, holding the position of senior researcher in the Microsurgery Division.

4. My practical experience in oncology and surgery began in 1992 and has been continuously proceeding to the present time. For the work in said field I was awarded the degree of candidate of medical sciences.

5. I am not an inventor of the invention disclosed in Application US N 09/890,496 titled "Use of polyacrylamide gel for forming a capsule in the tissue of the organism of a mammal, and a method of cultivating cells, and a method of treating oncological diseases and diabetes mellitus".

6. I have carried out the clinical study on tolerance of the xenogenic vaccination technique applied in the metastatic melanoma patients. Said study has been a part of Phase I clinical trials of said technique, which trials were carried out on the basis of the decision made by Committee for novel medical equipment of Ministry for Public Health of the Russian Federation (Protocol No. 9 of October 22, 2002).

For that purpose, said study included 21 patients having the histologically verified diagnosis of melanoma of the 4th stage (Addendum No. 2), condition after surgical treatment and chemoimmunotherapy, with localization of the primary focus on the body skin – 5 patients, on skin of limbs – 11 patients, on skin of face – 3 patients, and 2 patients with no primary focus detected. In the course of the study, the patients did not receive any additional antitumor treatment or other medication.

The tested means were 4% polyacrylamide gel (PAAG) and transplantable culture of murine melanoma B-16 cells, being an aseptically prepared suspension of live tumor cells of B-16 melanoma with a concentration of 50 million cells per 1 ml medium. The total volume of the preparation for single administration was 2 ml.

At the first stage, PAAG in the amount of 5 ml was injected subcutaneously the sub-clavicle back area of the patients under ultrasonic scanning (USS) monitoring. Prior to injection of the gel, the thickness of subcutaneous adipose tissue was evaluated by USS, which thickness generally was within the range of 5 to 20 mm. The gel was injected under USS monitoring into the center of the bulk of subcutaneous adipose tissue under local anesthesia with 2% lidocaine solution in quantity of 2 ml (Fig. 1). After injection of the gel, the ultrasonic pattern represented a hypoechogenic mass of a circular-oval shape, being 25 x 12 mm to 35 x 20 mm in size. The state of the depot so provided was assessed after 14 days after the gel had been injected. The ultrasonic pattern of the formed depot had two structural variants: the first one existed in the patients whose subcutaneous adipose tissue did not exceed 5 mm (Fig. 3); the echographic pattern of the formed depot represented a hyperechogenic cavity 4 – 5 mm thick, without sharp outlines and with no pronounced capsule. The second structural variant was found in the patients whose subcutaneous adipose tissue thickness was up to 20 mm (Fig. 4). The depot so provided appeared as a mass of an elongated-ovoid shape having the hypoechogenic structure, with a clearly distinct capsule having thickness of 0.5 mm at most. After preliminary assessment of formation of a capsule at the gel-injection site, B-16 preparation was administered in the volume of 2 ml via a syringe under USS monitoring on the 21-28th day. After the vaccine had been injected into the depot, the latter was retaining its shape and size, and the injected preparation appeared as a shapeless hypoechogenic mass without sharp outlines, having size of 15 to 17 by 6 to 8 mm, that did not exceed the boundaries of the formed depot (Fig. 2). The formed depot in some patients was assessed in three weeks following vaccination, and an insignificant increase in the size of the formed depot accompanied by hardening of the structure (Fig. 5) was observed. This treatment was applied to the patients only once. No toxic-allergic or inflammatory responses to injection of PAAG were detected.

In 13 patients, 62%, no allergic responses to injection of TMCC B-16 preparation were noticed. Two patients, 9%, exhibited a single rise of body temperature to 38° on the vaccination day. Local hyperemia in the injection site was observed in 4 patients – 19%. In two patients (9%) the allergic response in the form of skin rashes of the papular nature, accompanied with a feeble itch was noticed; the pattern used to normalize within 7 days, without administration of antihistamine drugs. Apart from the visual checkup and monitoring the condition of the patients, parameters of the patients' general and biochemical blood analyses were monitored. No changes

in the blood formula and biochemical indices were observed. No essential changes in the patients' general physical condition and in clinical-laboratory analyses were detected. Thus, evaluating the results of the carried-out clinical study on tolerance of this xenogenic vaccination technique, the absence of any severe local or general toxic responses after vaccination within the period of 1 to 8 months (Table 1) should be noted. The preventive efficiency of this xenogenic vaccination technique in terms of duration of the recurrence-free course and survival rate is hard to evaluate, nonetheless stabilization of the process and the absence of signs of further generalization during short-term follow-up in 19 (90%) patients among 21 patient should be noted, however 2 patients had further progress of the process resulted in fatal outcome. The foregoing constitutes the basis for continuation of studies in this filed aimed at determining the antitumor efficiency of this technique in melanoma patients.

7. Presently, basing on of the decision made by Committee for novel medical equipment of Ministry for Public Health of the Russian Federation (Protocol No. 1 of January 22, 2004), I am carrying out the studies within the frames of Phase II clinical trials of said technique for the purpose of determining the antitumor activity of subcutaneous injection of polyarylamide gel for maintaining xenogenic cells therein in the oncological patients in the prevention mode. Apart from the melanoma patients this study will include patients suffering from other oncological diseases amenable to immunological therapy, such as mammary gland cancer, kidney cancer, urinary bladder cancer.

8. The undersigned further declares that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the above-identified application or any patent issuing thereon.

Executed this 18 th day of May 2004.

Oleg Vladimirovich Matorin

Oleg Vladimirovich Matorin

Observation	Localization	The time PAAG was inserted	The time vaccination was administered	Concurrent response	Follow-up period
Malignant epithelio-cellular lentigomelanoma, 2nd-3rd level of invasion, 2 mm by Breslow	Body skin	13 05 03	10 06 03	Hyperthermia to 38° (on the day of vaccination)	6 months (negative course)
Malignant pigment-free melanoma, epithelio-spindle-cell melanoma, 5th level of invasion by Clark	Body skin	14 05 03	10 06 03	Local hyperemia during 2-3 days	7 months
Malignant ulcerated epithelio-spindle-cell melanoma, 3rd level of invasion, 5 mm thick by Breslow	Limb skin	26 05 03	01 07 03	none	12 months
Malignant pigmentary epithelio-spindle-cell melanoma, 3rd level of invasion by Clark, 2-mm thick by Breslow, at the background of lentigomelanoma	Body skin	28 05 03	01 07 03	none	6 months
Malignant epithelio-cellular melanoma, nodular growth type, with an expressed ulceration and necrosis across the surface, V level of invasion by Clark, 2-cm thick by Breslow	Limb skin	04 06 03	04 07 03	none	6 months
Metastasis of pigment-free melanoma	Without initial focus	09 06 03	01 07 03	none	4 months (negative course)
Metastasis of epithelio-cellular version of melanoma into stomach	Without initial focus	10 06 03	10 10 03	Allergic rashes on the body skin	3 months
Malignant pigment-free nevus-epithelio-cellular melanoma	Face skin	16 06 03	01 07 03	Allergic rashes on the body skin	6 months

Nodular epithelio-nevo-cellular pigmentary melanoma, non-ulcerated, 3rd level of invasion by Clark, 3.5-mm thick by Breslow	Limb skin	16 06 03	10 10 03	Local hyperemia	3 months
Lentigomelanoma, 2nd-3rd level of invasion by Clark, 1-mm thick by Breslow at the background of dysplasiac nevus with severe melanocytic lentiginosial dysplasia.	Body skin	09 07 03	10 10 03	None	3 months
Malignant nevo-cellular non-ulcerated melanoma, 3rd level of invasion by Clark, 2-mm thick by Breslow.	Limb skin	02 09 03	12 11 03	None	2 months
Malignant balloon-cell melanoma, non-ulcerated, 3rd level of invasion by Clark, 1-mm thick by Breslow	Limb skin	07 10 03	12 11 03	None	4 months
Melanoma, 3rd level of invasion	Limb skin	14 10 03	12 11 03	None	3 months
Epithelio-nevocellular lentigomelanoma, vertical growth stage, 3rd level of invasion by Clark, 2-mm thick by Breslow.	Limb skin	14 10 03	12 11 03	Hyperemia on the vaccination day	3 months
Epithelio- and spindle-cell pigmentary melanoma, 3rd level of invasion, 0.2-mm thick by Breslow.	Limb skin	15 10 03	12 11 03	None	3 months
No data as to the initial focus, metastasis of epithelio-cellular melanoma, partially with infiltration of the surrounding soft tissues	Limb skin	29 10 03	02 12 03	None	2 months

Surface-expanding malignant pigmentary non-ulcerated melanoma, 2nd level of invasion by Clark, thickness of tumour by Breslow less than 0.75 mm	Face skin	29 10 03	02 12 03	None	2 months
Nodular epithelio-cellular melanoma, 5th level of invasion by Clark, 6-mm thick by Breslow	Limb skin	29 10 03	02 12 03	None	2 months
Epithelio-cellular pigmentary melanoma, 1st level of invasion by Clark, less than 0.75 mm thick by Breslow	Limb skin	11 11 03	23 12 03	None	1 month
Epithelio-cellular pigmentary melanoma with ulceration (3rd level of invasion by Clark, 3-mm thick by Breslow	Body skin	25 11 03	23 12 03	Local hyperemia	1 month
Malignant melanoma	Face skin	25 11 03	23 12 03	Local hyperemia	1 month

1. ***Ignatenkov Igor Valentinovich, 36***

Clinical diagnosis: Back skin melanoma. Condition after the combined treatment carried out in 2001. The process progressed in 2002 by metastasis into liver. Condition after 4 courses of polychemotherapy. Further progress of the process occurred in April 2003 in the form of development of subcutaneous metastases in the area of navel, recurrence in the area of post-operation scar, lesions of lymph node in the left armpit and supra-clavicle area, renewed metastasis affecting the liver. Condition after excision of the subcutaneous metastasis in the navel area after the 1st course monochemotherapy. Further progress of the tumour process. Condition subsequent to symptomatic treatment.

Histology: L 3336-40. The back skin has a pigmentary mass. Macro: the skin patch having size of 13 x 11 cm, with subcutaneous fat. On the skin, in the center of the patch there is a spot of black colour, with irregular outlines, shaped in the form of a "butterfly", 5 x 4.5 cm, the edge of the spot has a plaque 1.5 cm in diameter. Micro: In conformity with the spot – a malignant epithelio-cellular lentigomelanoma, 2nd-3rd level of invasion, with vast areas of spontaneous resorption. In conformity with the plaque – the malignant epithelio-cellular ulcerated melanoma, 3rd level of invasion, 2-mm thick by Breslow. Excised within limits of healthy tissues.

Date of insertion of PAAG (3 ml) – 13.05.03

Vaccination date – 10.06.03

Responses – one-time rise of body temperature to 38°C in the evening of vaccination day.

2. Solodovnik Zienayida Dmitriyevna, 57

Clinical diagnosis: Skin melanoma of the anterior abdominal wall, stage III, pT4N0M0. Condition subsequent to the combined treatment carried out in 2002 – 2003. Progress of the process in the form of metastasis into the left groin lymph node in 02.03. Condition subsequent to the surgical treatment carried out in 06. 03, after the 2nd course of monochemotherapy.

Histology:

No. L 65991-66002 – the malignant pigment-free, epithelio-spindle cell melanoma, with the presence of balloon cells, with a vast deep ulceration, frequent mitosis figures in sight, necrosis fields through the entire thickness of the tumour node, growth into the subcutaneous fat (5th level of invasion by Clark). In the plaque disposed at the tumour node edge – the malignant pigmentary epithelio-cellular melanoma, non-ulcerated, 0.2 cm thick (3rd level of invasion by Clark). The tumour has been excised within the limits of healthy tissues.

No. M 5982-95: in two lymph nodes – metastases of the pigment-free epithelio-spindle-cell melanoma, with almost complete replacement of the lymph tissue with the tumour tissue, infiltration of subcutaneous fat; in the remaining eight lymph nodes, sampled from the excised tissue fragments – hyperplasia of lymph tissue.

PAAG insertion date (3 ml) – 14.05.03

Vaccination date – 10/06.03

Responses – local hyperemia during 2 – 3 days.

3. Plechkova Tayisa Mikhaylovna, 63

Clinical diagnosis: Primary-multiple synchronous tumours: 1. Skin melanoma on the left shin, stage I, pT2N0M0. Condition subsequent to the combined treatment carried out in 06.2003, in the course of immunotherapy. 2. Liposarcoma of soft tissues on the right politeal area, stage Ia, T1bN0M0G1. Condition subsequent to surgical treatment carried out in 06.2003.

Histology: No. M6537-55:

1. The malignant ulcerated epithelio-spindle-cell melanoma, the 3rd level of invasion, 5-mm thick by Breslow. Excised within limits of healthy tissues. Any melanoma has not been detected in all studied lymph nodes.
2. Mixoidal liposarcoma. Excised within limits of healthy tissues.

PAAG insertion date (3 ml) – 26.05.03

Vaccination date – 01.07.03

Responses – none

4. Zhouravlyov Vladimir Mikhaylovich, 57

Clinical diagnosis: abdomen skin melanoma, with intracutaneous metastasis of stage IV, pT3aN0M1a. Condition subsequent to the surgical treatment carried out in 06.03, in the course of chemoimmunotherapy.

Histology: No. M 8050-53:

1. The malignant pigmentary epithelio-spindle-cell melanoma, 3rd level of invasion by Clark, 2-mm thick by Breslow, at the background of lentigomelanoma, at the edges – with foci of spontaneous resorption of the melanoma.
2. Intracutaneous metastasis of the malignant epithelio-spindle-cell melanoma. Excised within limits of healthy tissues.

PAAG insertion date (3 ml) – 28.05.03

Vaccination date – 01.07.03

Responses – none

5. Gorkina Antoniena Dmitriyevna, 55

Clinical diagnosis: The malignant epithelio-cellular melanoma on the right shin skin, with metastases into the groin lymph nodes of phase III, pT4N2M0, condition after surgical treatment carried out in 03.2003; after radiation therapy of the right groin-thigh area carried out in 05-06.03. The process progressed in May 2003 in the form of development of intracutaneous metastases on the right lower limb; Condition subsequent to the 1st course of monochemotherapy. Further progress of the tumour process occurred in 08.03.

Histology: No. L 91071-90: The malignant epithelio-cellular melanoma, the nodular form of growth, with an expressed ulceration and surface necrosis, V level of invasion by Clark, 2-cm thick by Breslow, with metastasis into the groin lymph node having size of 5 x 4 cm, with complete replacement of the lymph tissue with the tumour tissue and infiltration of the subcutaneous fat. In the remaining 13 studied lymph nodes of the regional zones – hyperplasia of the lymph tissue.

PAAG insertion date (3 ml) – 04.06.03

Vaccination date – 04.07.03

Responses – none

6. Shved Pyotr Fyodorovich, 60

Clinical diagnosis: The malignant skin melanoma, stage IV, generalization of the process in the form of metastases into brain, liver, lungs, mediatinum lymph node, para-aortic area lymph node, celiac trunk area. Condition subsequent to surgery treatment carried out in May 2003. Condition subsequent to 1st course of monochemotherapy. Negative course.

Histology: (cons. No. 584/03): metastases of pigment-free melanoma.

PAAG insertion date (6 ml) – 09.06.03 (subfascially, monitored by ultrasonic scanning)

Vaccination date – 01.07.03

Responses – none

7. Torbiena Rayisa Romanovna, 67

Clinical diagnosis: Melanoma, without any revealed initial focus, stage IV: subcutaneous metastasis in the right iliac area, metastasis into lymph node of the right lateral surface of the neck, metastases into the lower one-third of stomach. Condition subsequent to 2 courses of polychemotherapy carried out in 03-04.03; after excision the post-operative scar in the right iliac area and lymph nodes on the right lateral surface of the neck done in 05.03; subsequent to endoscopic excision of the tumour in lower one-third of stomach and a broad

excision of the post-operative scar in the right iliac area. Further progress of the tumour process in the form of recurrence on the right side of the neck.

Histology (when discharged) No. 26799-812/03 – no data as to any malignant growth (post-operative scar); No. 26925-32/03 – metastases of the epithelio-cellular version of melanoma into stomach.

PAAG insertion date (6 ml) – 10.06.03

Vaccination date – 10.10.03

Responses – allergic response in the form of rashes on the skin of the right elbow area and on the pubic skin area, accompanied with a feeble itch. The pattern normalized in 7 days.

8. Bouldakov Serghey Vladimirovich, 44

Clinical diagnosis: Melanoma of the right superior eyelid conjuctiva. Condition subsequent to surgical treatment carried out in 07.02. Continued growth, metastases into lymph nodes in neck on the right side. Condition subsequent to surgical treatment carried out in 06.03.

Histology: No. M3923-37: The malignant pigment-free nevo-epithelio-cellular melanoma. In 6 lymph nodes of the regional zones – hyperplasia of lymph tissue.

PAAG insertion date (6 ml) – 16.06.03 (subfascially, monitored by ultrasonic scanning)

Vaccination date – 01.07.03

Responses – allergic response in the form rashes of multitudinous nature, which rashes partially merged and disposed predominantly on the skin of the right half of the body; development of new spots and an increase in size of the already existing spots were accompanied by a rise of body temperature to subfebrile values and a manifest itch. The pattern normalized in 7-10 days.

Repeated vaccination into the pre-formed capsule – 12.11.03.

Response – a manifest oedemas and hyperemia of tissues on the vaccination site, generally 11 x 8 cm in diameter, persisting during 4 days.

9. Svetlova Svetlana Vasil'yevna, 53

Clinical diagnosis: Right shoulder skin melanoma, stage II, pT3bN0M0. Condition subsequent to surgical treatment carried out in 01.02. Progress of the tumour process in the form of metastases into the right armpit lymph node occurred in 05.03. Condition subsequent to surgical treatment carried out in 07.03, in the course of chemoimmunotherapy.

Histology: No. L 35134-35: The nodular epithelio-nevocellular melanoma, non-ulcerated, 3rd level of invasion by Clark, 3.5-mm thick by Breslow. Excised within limits of healthy tissues.

PAAG insertion date (6 ml) – 16.06.03

Vaccination date – 10.10.03

Responses – local hyperemia during 2 – 3 days

10. Semenyuk Valentiena Ivanovna, 64

Clinical diagnosis: Skin melanoma of the left chest wall, stage I, pT2N0M0. Condition subsequent to surgical treatment carried out in 06.03.

Histology No. M 8035-38: Lentigomelanoma, 2^{nd}-3^{rd} level of invasion by Clark, 1-mm thick by Breslow, at the background of dysplasiac nevus with severe melanocytic lentiginosial dysplasia. Excised within limits of healthy tissues.

PAAG inserton date (6 ml) – 09.07.03

Vaccination date – 10.10.03

Responses – none

11. Savicheva Ol'ga Alexandrovna, 62

Clinical diagnosis: primary multicentric cancer: Thyroid gland cancer at the background of adenomatopsis of stage II, T2N0M0. Condition subsequent to surgical treatment carried out in 10.03, in the course of radiation therapy. Left thigh skin melanoma of stage IIA, T2N0M0. Condition subsequent to surgical treatment carried out in 06.03.

Histology: M 6008-22 – the malignant nevocellular non-ulcerated melanoma, 3^{rd} level of invasion by Clark, 2-mm thick by Breslow. No tumour elements in the resection edges. No metastases into lymph nodes.

PAAG insertion date (6 ml) – 02.09.03

Vaccination date – 12.11.03

Responses - none

12. Stakhova Valentiena Mikhaylovna

Clinical diagnosis: Left shin skin melanoma, stage I, pT2N0M0. Condition subsequent to surgical treatment carried out in 09.03. Progress of the process occurred in 09.03. Condition subsequent to surgical treatment.

Histology: No. K 76353-54 – the malignant balloon cell melanoma, non-ulcerated, 3^{rd} level of invasion by Clark, 1-mm thick by Breslow, without lymphoid infiltration in the base. Excised within limits of healthy tissues.

PAAG insertion date (6 ml) – 07.10.03

Vaccination date – 12.11.03

Responses – none

13. Petrov Igor Ghertroudovich, 50

Clinical diagnosis: skin melanoma of the upper one-third of the left shoulder, with metastasis into lymph nodes of the right armpit area, III, pT2N1M0. Condition subsequent to the combined treatment carried out in 2000-2001. Recurrence in the post-operative scar area occurred in 12.01. Condition subsequent to the combined treatment.

Histology:

PAAG insertion data (6 ml) – 14.10.03

Vaccination date – 12.11.03

Responses – none

14. Babayev Anatoliy Kouzmich, 58

Clinical diagnosis: Skin melanoma of the left thigh, stage II, pT3N0M0. Condition subsequent to surgical treatment carried out in 1998. Progress of the process occurred in 07.03 in the form of metastasis lesions in lymph node of the left groin area. Condition subsequent to the combined treatment.

Histology: cons. No. 1043/03:

- No B 5622-30/88 epithelio-nevocellular lentigomelanoma, vertical phase of growth, 3rd level of invasion by Clark, 2-mm thick by Breslow.
- No. B 8996-9000/03 fragmented lymph node with melanoma metastasis of the similar structure, almost with the complete replacement of the intrinsic tissue; making any judgment as to the capsule invasion seems not possible.

PAAG insertion date (6ml) – 14.10.03

Vaccination date – 12.11.03

Responses – a rise of body temperature in the evening of the vaccination date to 38.0°C.

15. Traktierova Tatyana Niekolayevna, 53

Clinical diagnosis: Skin melanoma on the left foot third finger, stage II, pT3N0M0. Condition subsequent to combined treatment carried out in 04.02 – 04.03. Progress of the process in the form of metastasis-lesion of the left groin lymph node. Condition subsequent to combined treatment carried out in 04.03 – 06.03.

Histology: cons. No. 1153/03 – epithelio- and spindle-cell pigmentary melanoma, 3rd level of invasion by Clark, 0.2-mm thick by Breslow.

PAAG insertion date (6 ml) – 15.10.03

Vaccination date – 12.11.03

Responses – rheumatic pain feeling in bones during 2 days

16. Skyayev Yuriy Mouratovich, 57

Clinical diagnosis: Skin melanoma of the right thigh. Condition subsequent to laser coagulation done in 2001. Progress of the process occurred in 09.03. Condition subsequent to surgical treatment. Negative course. Condition in the course of monochemotherapy.

Histology: No. M 11696-735 – in 36 lymph nodes – metastases of epithelio-cellular melanoma, partially with infiltration of the surrounding soft tissues.

PAAG insertion date (6 ml) - 29 10 03

Vaccination date – 02 12 03

Responses – none

17. Gordeyeva Yevgheniya Vladimirovna, 31

Clinical diagnosis. Skin melanoma of the left cheek, stage I, pTN0M0. Condition subsequent to surgical treatment carried out on 25.06.03.

Histology: No. M 8189-93 – surface-expanding malignant pigmentary non-ulcerated melanoma, 2nd level of invasion by Clark, tumour thickness by Breslow is less than 0.75 mm. On the tumour periphery, the focal lymphoid concentration is observed; the tumour was excised within limits of healthy tissues.

PAAG insertion date (6 ml) – 20.10.03

Vaccination date – 02.12.03

Responses – none

18. Chernyavskaya Svetlana Griegoryevna, 31

Clinical diagnosis: Skin melanoma of the lower one-third of the right shin front surface, stage II, pTN0M0. Condition subsequent to the surgical treatment, in the course of immunotherapy.

Histology: No. M 0916-19 – nodular epithelio-cellular melanoma, 5th level of invasion by Clark, 6-mm thick by Breslow. Any tumour growth at the resection edges has not been detected.

PAAG insertion date (6 ml) – 29.10.03

Vaccination date – 02.12.03

Responses – none

19. Gheniena Ol'ga Vyacheslavovna, 23

Clinical diagnosis: Skin melanoma of the right thigh, stage I, pT1N0M0. Condition subsequent to the surgical treatment 16.10.03.

Histology: epithelio-cellular pigmentary melanoma. 1st level of invasion by Clark, thickness by Breslow is less than 0.75 mm.

PAAG insertion date (6 ml) – 11.11.03

Vaccination date – 23.12.03

Responses – none

20. Krylova Yulia Sergheyevna, 23

Clinical diagnosis: back skin melanoma, pT3aN0M0. Condition subsequent to the surgical treatment 20.10.03.

Histology: No. M 19528-38

Macro: 1) Plaque-shaped mass having size 2 x 0.9 x 0.1 cm; 2) Skin patch, in the center – the plaque-shaped mass of 0.7 cm; 3) Skin, in the center a pigment spot of 0.4 cm.

Micro: 1) epithelio-cellular pigmentary melanoma, ulcerated (3rd level of invasion by Clark, 3-mm thick by Breslow, in the vicinity – a complex nevus having foci of melanocytic lentiginosial dysplasia; 2) A complex pigmentary nevus; 3) Intradermal pigmentary nevus.

PAAG insertion date (6 ml) – 25.11.03

Vaccination date – 23.12.03

Responses – hyperemia on the vaccination site during 4-5 days.

21. Zaytseva Leonarda Vyacheslavovna

Clinical diagnosis: Melanoblastoma of the right eyeball choroidea. Condition subsequent to surgical treatment carried out in 1978. Progress of the process occurred in 2002; metastasis into liver. Condition subsequent to chemoimmunotherapy. Stabilization of the process. Condition in the course of treatment by "muestoforan"

Histology: (on the date of discharge from A.V. Vishnevskiy Institute of Surgery) malignant melanoma.

PAAG insertion date (6 ml) – 25.11.03

Vaccination date – 23.12.03

Responses – hyperemia on the vaccination site during 4 – 5 days.

Fig. 1 Ultrasonic scanning pattern of the formed depot of PAAG after one day subsequent to insertion.

Fig. 2 - Ultrasonic scanning pattern after one day subsequent to insertion of B-16 cell culture

Fig. 3 – Versions of the ultrasonic scanning pattern on the site of insertion of B-16 cell culture, thickness of subcutaneous fat being up to 5mm.

Fig. 4 – Versions of the ultrasonic scanning pattern on the site of insertion of B-16 cell culture, thickness of subcutaneous fat being up to 20 mm.

Fig. 5 – Modification of the ultrasonic scanning pattern on the site of insertion of B-16 cell culture.

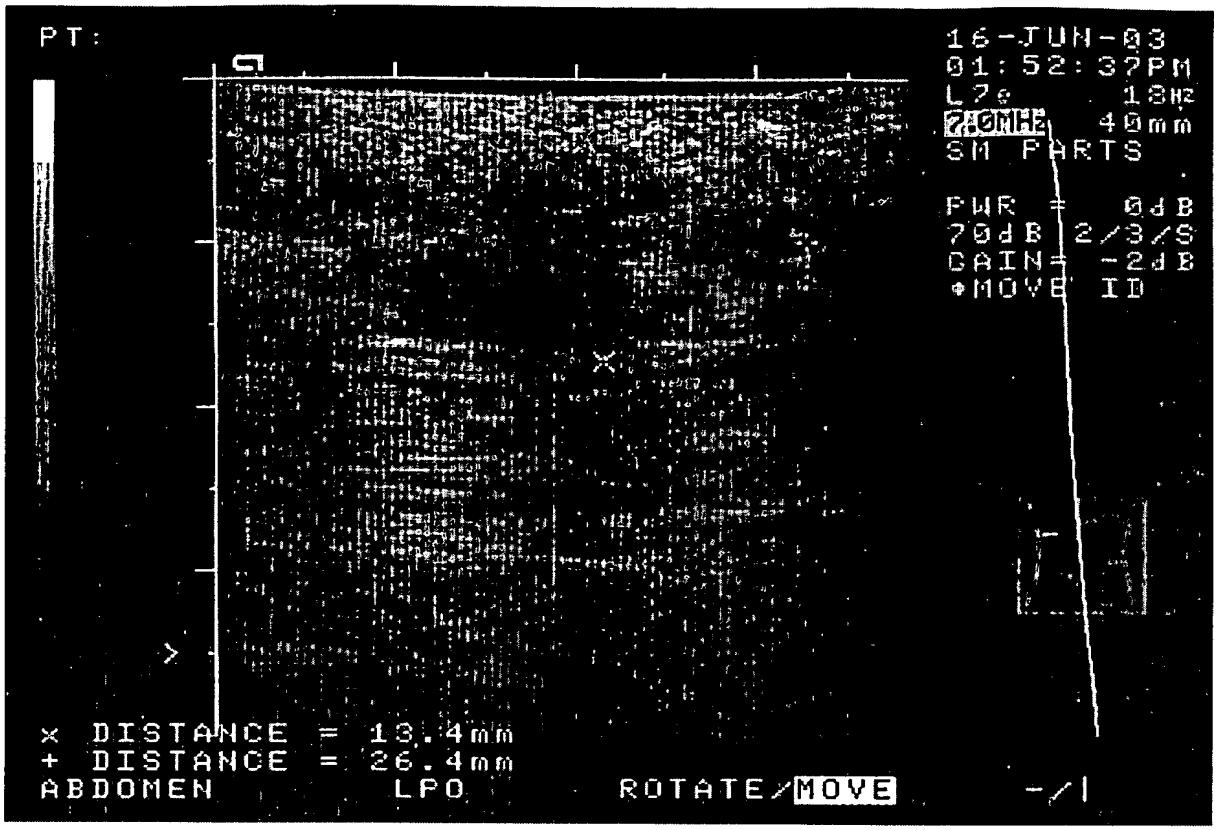

Fig. 1. Ultrasonic scanning pattern of the PAAG depot formed after 1 day following PAAG injection.

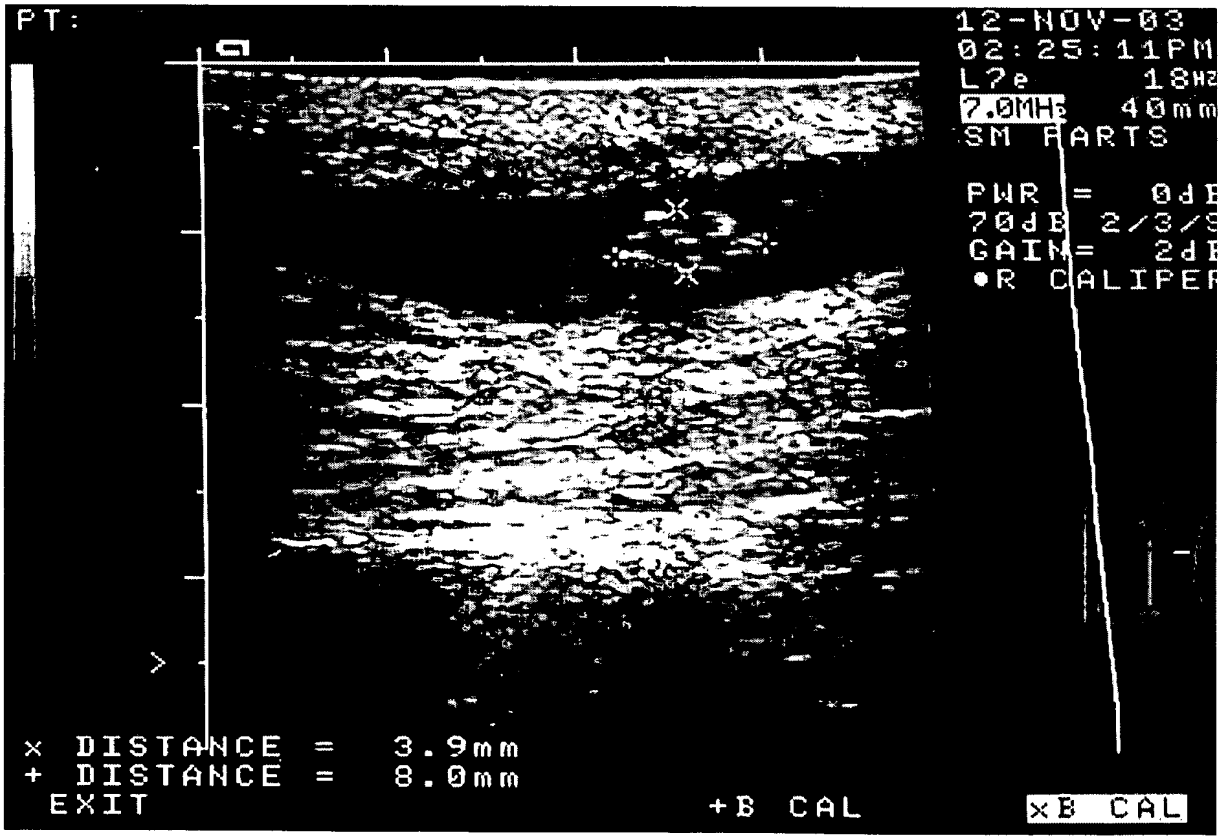

Fig. 2. Ultrasonic scanning pattern after 1 day following injection of B-16 cell culture.

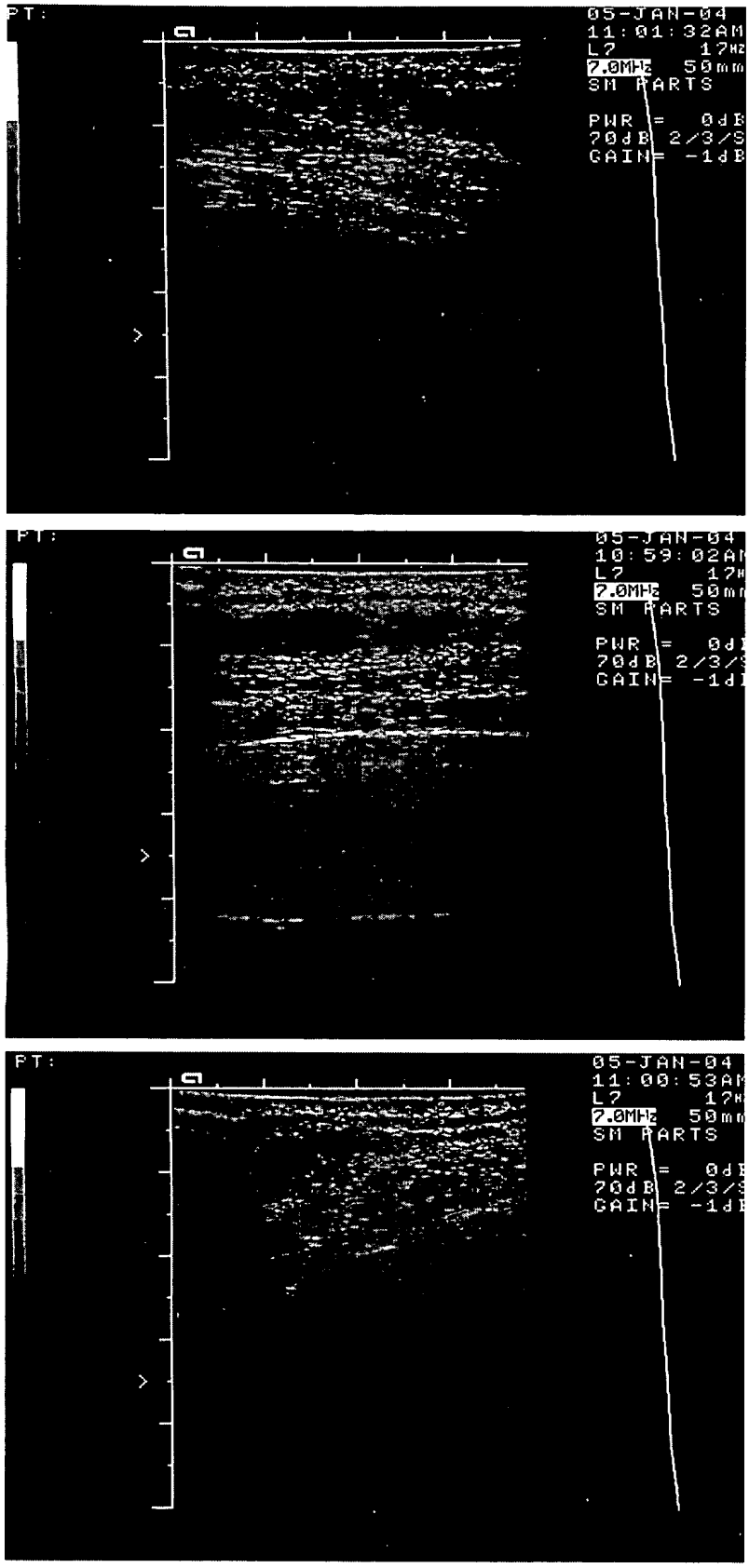

Fig. 3. Versions of the ultrasonic scanning patterns of the B-16 cell culture injection site when the thickness of subcutaneous adipose tissue was up to 5 mm.

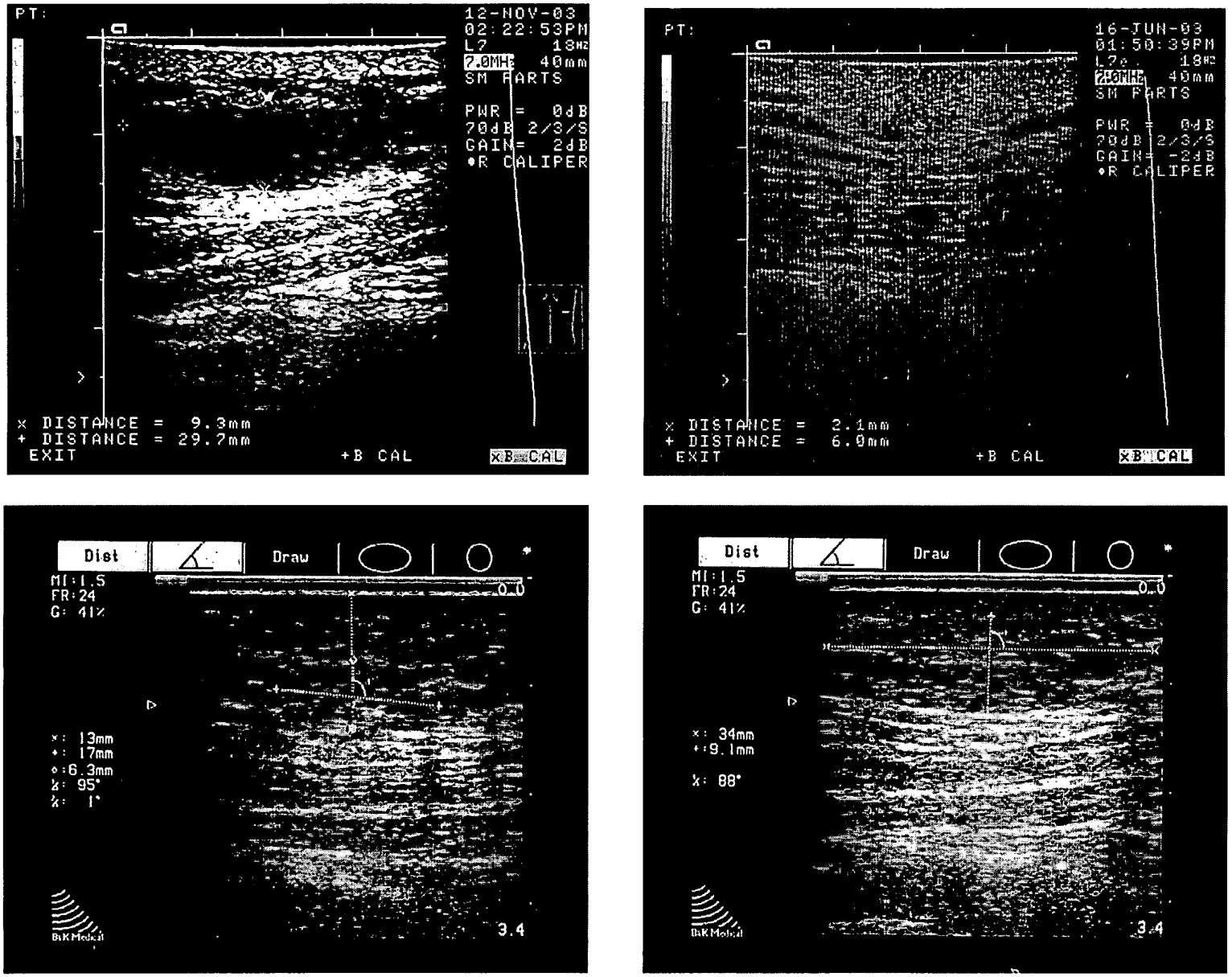

Fig. 4. Versions of the ultrasonic scanning patterns of the B-16 cell culture injection site when the thickness of subcutaneous adipose tissue was up to 20 mm.

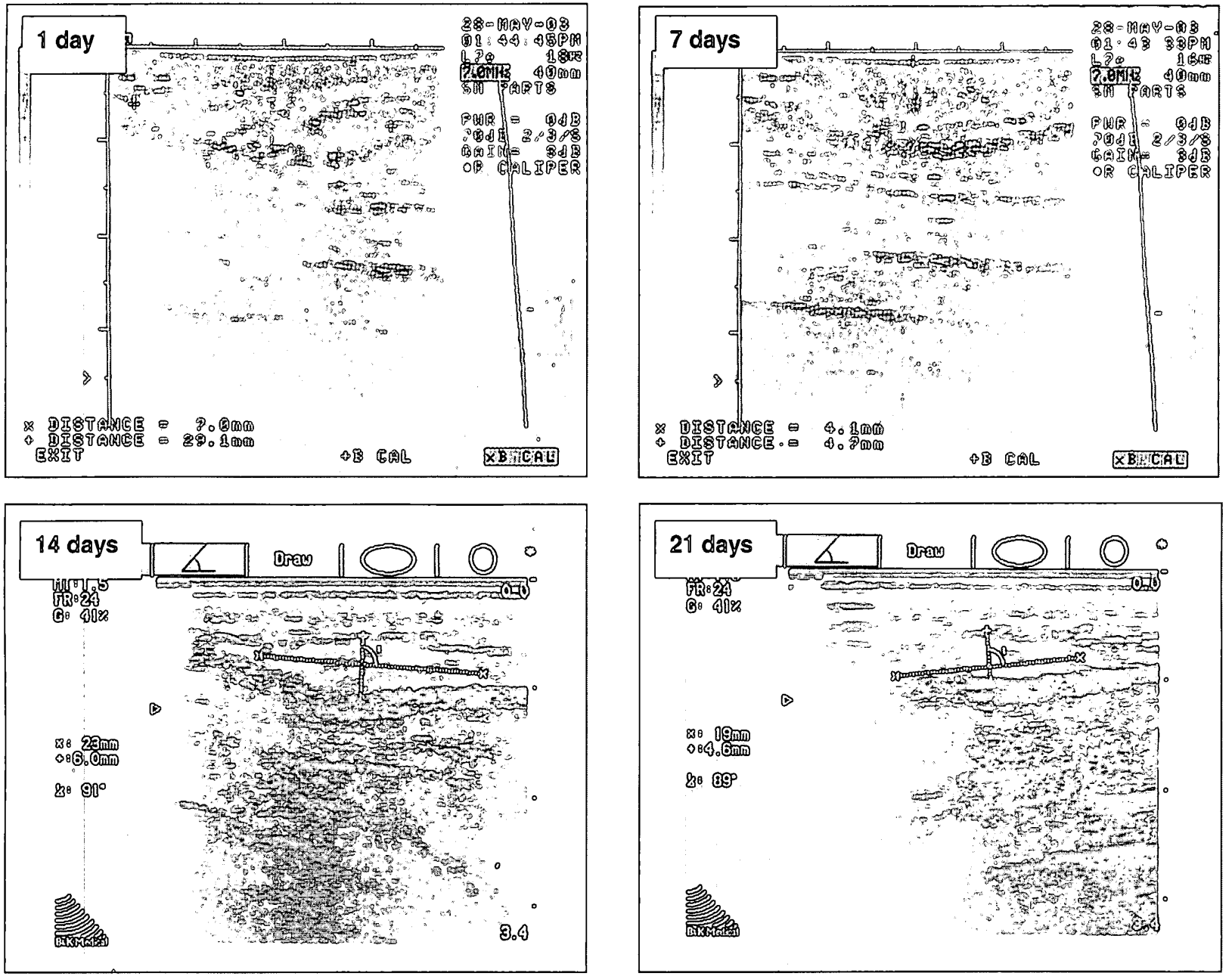

Fig. 5. Time-dependent changes in the ultrasonic scanning pattern of the B-16 cell culture injection site.